UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/687,674	10/17/2003	Bryon E. Petersen	5853-310	9364

7590 04/24/2006

Stanley A. Kim, Ph.D., Esq.
Akerman Senterfitt
Suite 400
222 Lakeview Avenue
West Palm Beach, FL 33402-3188

EXAMINER	
AFREMOVA, VERA	
ART UNIT	**PAPER NUMBER**
1651	

DATE MAILED: 04/24/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/687,674	PETERSEN ET AL.	
	Examiner	Art Unit	
	Vera Afremova	1651	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *14 February 2006*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-27* is/are pending in the application.

4a) Of the above claim(s) *12-27* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-11* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *12/02/2005*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Claims 1-27 are pending.

Claims 12-27 were withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to nonelected inventions, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in the reply filed on 9/01/2005.

A complete reply to the final rejection must include cancellation of nonelected claims or other appropriate action (37 CFR 1.144) See MPEP § 821.01.

Claims 1-11 are under examination in the instant office action.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

Claims 1, 4-7, 9-11 remain rejected under 35 U.S.C. 102(e) as being anticipated by US 2002/0182728 (Ramiya et al.) as explained in the prior office action and repeated herein.

Claims are directed to a method for differentiating mammalian bone marrow cells into endocrine hormone-producing cells wherein the method comprises step of providing bone marrow cells, step of culturing the bone marrow cells in a low glucose-medium comprising DMSO and step of culturing the bone marrow cells in a high glucose-medium comprising serum

under condition and for a sufficient time to promote differentiation of the cells into endocrine hormone-producing cells. Some claims are further drawn to the endocrine hormones being insulin, glucagon, somatostatin and/or pancreatic polypeptide. Some clams are further drawn to the use of high glucose-medium with 25 mM glucose, DMEM and fetal bovine serum. Some clams are further drawn to culturing cells for approximately 7 days.

US 2002/0182728 (Ramiya et al.) teaches a method for trans-differentiation of bone marrow cells into cells of pancreatic lineage that express genes and markers for endocrine hormone production including insulin, glucagon, somatostatin and pancreatic polypeptide (see par. 0049, 0051, 0052, 0062). The method comprises step of providing bone marrow cells including HSCs and/or MSCs and steps of sequential culturing the bone marrow cells in culture media A and B under conditions and for a sufficient time to promote differentiation of the cells into cells of pancreatic lineage (0049) within the meaning of the instant claims. In particular, the medium intended for trans-differentiation contains DMEM, fetal bovine serum and 4500 mg/L (25 mM) glucose (see table 1A) and, thus, the trans-differentiation medium provides for the same "high-glucose " amount as required by the claimed invention. The cells are cultured in sequential media or they are cultured for 2 days in first medium and than up to 14 days in second medium. Thus, before addition of a second medium an amount of glucose a first culture medium was lower than in the added second medium. The cited patent also discloses that cells were thawed before exposure to trans-differentiation medium. Therefore, cells were exposed to a cryoprotective agent. DMSO is a most common cryoprotectant agent. Thus, there is a reasonably believe that bone marrow cells were cultured and exposed to the same media and/or agents as encompassed by the claimed method, particularly in view that the final effects of manipulating

bone marrow cells such as differentiation into cells of pancreatic linage are identical as disclosed by the cited patent and as claimed. Therefore, the cited method and the claimed method are identical and the cited patent is considered to anticipate the claimed invention.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1-11 remain rejected under 35 U.S.C. 103(a) as being unpatentable over US 2002/0182728 (Ramiya et al.) taken with Yang et al. (IDS reference; PNAS, June 2002, Vol. 99, No. 12, pages 8078-8083), Petersen et al. (IDS reference; Science, may 1999, Vol. 284, pages 1168-1170), US 2003/0104997 (Black et al.) and US 6,458,589 (Rambhatla et al.) as explained in the prior office action and repeated herein.

Claims are directed to a method for differentiating mammalian bone marrow cells into endocrine hormone-producing cells wherein the method comprises step of providing bone marrow cells, step of culturing the bone marrow cells in a low glucose-medium comprising DMSO and step of culturing the bone marrow cells in a high glucose-medium comprising serum under condition and for a sufficient time to promote differentiation of the cells into endocrine hormone-producing cells. Some claims are further drawn to the endocrine hormones being insulin, glucagon, somatostatin and pancreatic polypeptide. Some clams are further drawn to the use of low glucose-medium with 5.5 mM glucose. Some clams are further drawn to the use of

high glucose-medium with 25 mM glucose, DMEM and fetal bovine serum. Some clams are further drawn to culturing cells for approximately 7 days.

US 2002/0182728 (Ramiya et al.) teaches a method for trans-differentiation of non-pancreatic stem cells including mammalian or human bone marrow HSCs, bone marrow MSCs and liver oval cells into endocrine hormone expressing cells (par. 0032) by culturing bone marrow cells in sequential media under condition and for a sufficient time to promote differentiation (par. 0049, 0051, 0052, 0059-0063) including the use of media with 25 mM glucose, DMEM and fetal bovine serum.

In particular, the cited document US 2002/0182728 is silent about sequential use of "low" and "high" glucose media for trans-differentiation of non-pancreatic cells and for stimulation of endocrine hormone production. However, the reference by Yang et al. teaches that non-pancreatic cells such as hepatic oval cells are induced for trans-differentiation by switching cells from a first medium with about 5.5 mM to a second medium with 23 mM (page 8078, col. 2, par. 4, last 5 lines). Further, the reference by Petersen et al. provides teaching that bone marrow cell population contains oval cells that are hepatic stem cells (entire document including title and abstract).

In particular, the cited document US 2002/0182728 is silent about DMSO as an agent promoting differentiation. However, US 2003/0104997 (Black et al.) teaches DMSO as an agent that is a precursor differentiation-inducing compound for bone marrow cells in a differentiation pathway from bone marrow cells into insulin-secreting cells (abstract). In addition, US 6,458,589 (Rambhatla et al.) also teaches DMSO as a differentiation or maturation agent for

hepatic stem cells (col.17, lines 45-47). The hepatic stem cells are found in bone marrow cells population as taught by Petersen et al.

Therefore, it would have been obvious to one having ordinary skill in the art at the time the claimed invention was made to stimulate differentiation of bone marrow cells by switching the bone marrow cell culture from low glucose medium to high glucose medium with a reasonable expectation of success in differentiation of bone marrow cells into endocrine hormone producing cells because bone marrow cell population have been demonstrated to differentiate into endocrine hormone expressing cells under appropriate conditions, because bone marrow cell population is a source of stem cells of various cell lineages including hepatic stem cells such as oval cells that are known to be stimulated to produce endocrine hormones by switching from low to high glucose culture media as adequately demonstrated by the cited prior art. Thus, the claimed invention as a whole was clearly *prima facie* obvious, especially in the absence of evidence to the contrary.

Therefore, it would have been obvious to one having ordinary skill in the art at the time the claimed invention was made to induce and/or to stimulate differentiation of bone marrow cells by exposing the cells to DMSO with a reasonable expectation of success in differentiation of bone marrow cells into endocrine hormone producing cells because DMSO has been taught and/or suggested as a precursor differentiation inducing agent for the bone marrow cells and because DMSO has been taught and/or suggested as differentiation/maturation agent for the oval cells that are found within the bone marrow cell population as adequately demonstrated by the cited prior art. Thus, the claimed invention as a whole was clearly *prima facie* obvious, especially in the absence of evidence to the contrary.

The claimed subject matter fails to patentably distinguish over the state art as represented be the cited references. Therefore, the claims are properly rejected under 35 USC § 103.

Response to Arguments

Applicant's arguments filed 2/14/2006 have been fully considered but they are not found persuasive.

In response to applicant's argument that the references fail to show certain features of applicant's invention, it is noted that the features upon which applicant relies are not recited in the rejected claim(s). The specific culturing conditions as argued are: the use of 1% DMSO for culturing bone marrow cells at specific seeding densities in a serum-free medium with "low" glucose for 3 days before transfer and culturing cells into "high" glucose and serum-containing medium for 7 days. Moreover, the claims do not recite what amounts are encompassed by claimed terms "low" and "high" glucose. Although the claims are interpreted in light of the specification, limitations from the specification are not read into the claims. See *In re Van Geuns*, 988 F.2d 1181, 26 USPQ2d 1057 (Fed. Cir. 1993).

Conclusion

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after

the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Vera Afremova whose telephone number is (571) 272-0914. The examiner can normally be reached from Monday to Friday from 9.30 am to 6.00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael Wityshyn can be reached at (571) 272-0926.

The fax phone number for the TC 1600 where this application or proceeding is assigned is (571) 273-8300.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Technology center 1600, telephone number is (571) 272-1600.

Vera Afremova

AU 1651

April 20, 2006

VERA AFREMOVA

PRIMARY EXAMINER